

## REMARKS

Claims 39-42, 48-51, 45-80, and 82-142 are pending. Herein, Applicants have amended claims 94 and 95 by replacing "consisting essentially of" with "comprising". No new matter has been added by way of this amendment.

Applicants appreciate the indication made in Paper 23 that claims 39-42, 48-51, 54-66, 96-100, and 100-142 are allowable. Applicants respectfully request reconsideration of the remaining claims in view of the following remarks.

A. The Rejected Claims Are Non-Obvious.

Claims 67, 68, 74, 75, 84, 85, 92, 94, 95, and 101, and dependent claims 69-73, 76-80, 82, 83, 86-91, and 93, stand rejected or objected to under 35 U.S.C. § 103(a) as being unpatentable over New England Biolabs adaptor oligonucleotide Products #1101-1108, in view of a reference by Sumner, *et al.* Applicants respectfully traverse this rejection, and lodge their disagreement with the characterization in Paper 23 that the Sumner, *et al.* reference describes "primer amplification wherein the homology is minimal and generally is functional when at least 3 hybridized base pairs exist between the primer [and target]".

To establish a *prima facie* case of obviousness premised on a combination of references, both a motivation to combine the references as suggested and a reasonable expectation of achieving the invention must be demonstrated. No such demonstration has been made in this case.

The Sumner, *et al.* reference reports certain minimal homology requirements for oligonucleotides useful in PCR-based cloning processes. In particular, the reference states that "Primers with a length between 17-20nt need at least three homologous nucleotides at their 3'-end for successful priming." The reference also reported that weak priming was obtained using a long primer, *i.e.*, a primer comprised of 36 nucleotide bases, the two 3'-most of which were homologous to the target sequence. Based on these results, the reference suggested several criteria for designing oligonucleotides for use in PCR-based cloning, including that "the length [of any such

oligonucleotide] should preferably be between 20-24nt and the three 3' nucleotides should match [the target] completely."

Applicants respectfully submit that the criteria set forth in the Sumner, *et al.* reference regarding primer length and homology for PCR-based cloning is clear, namely that such oligonucleotides should be at least 17 nucleotides, preferably 20-24 nucleotides, in length, and that the three 3'-most nucleotides of such primers should be homologous with the target. Neither of New England Biolabs' Products #1106 nor #1101 satisfy these criteria. Product #1106 is 16 nucleotides in length, while product #1101 is only 10 nucleotide bases long. Moreover, in the comparisons made in Paper 23, only Product #1101 is depicted as having three 3' completely complementary nucleotides. Thus, both of the New England Biolabs' products discussed in Paper 23 fall below the range of oligonucleotide sizes discussed in the Sumner, *et al.* reference, and only one of these products, #1101 (which consists only 10 nucleotides in all, and only six of which are complementary to SEQ ID NO:22), has three 3' complementary nucleotides, and no where is it taught or suggested that either of Products #1106 or #1101 could be used as a PCR amplification primer.

Applicants also wish to note for the record that the Sumner, *et al.* reference concerned primer oligonucleotides useful in PCR-based cloning processes. In contrast, the cited New England Biolabs' Products #1101-1108 are described for use as adaptors in ligation reactions; they are not described or suggested to be useful as primers for nucleic acid amplification processes. Applicants also note that the Sumner, *et al.* reference discusses relative homology between a primer and its target, whereas the comparison illustrated in Paper 23 shows relative complementarity between two of Applicants' claimed sequences and two New England Biolabs' adaptor constituents.

Given the foregoing, Applicants respectfully submit that an ordinarily skilled artisan would not be motivated to use any of New England Biolabs' oligonucleotide adaptor Products #1101-1108 as primers in the PCR-based cloned procedures discussed in the Sumner, *et al.* reference. Indeed, Applicants submit that the Sumner, *et al.* reference actually teaches away from such a combination, given the differences in oligonucleotide size and homology. Moreover, even if such a motivation existed, combining the references as suggested in Paper 23 would not reasonably be expected to work because the Sumner, *et al.* reference reports a minimum PCR primer length of 17 nucleotides.

However, Product #1106 is only 16 nucleotides in length, and Product #1101 is six nucleotides shorter still. Thus (and assuming *arguendo* that Products #1101-1108 can be used as PCR cloning primers), the ordinary artisan would not expect primers of 10 and 16 nucleotides to work in the process discussed in the Sumner, *et al.* reference. This position is further buttressed upon inclusion of the criterion from the Sumner, *et al.* reference that requires homology between the three 3' nucleotides of the primer and its target.

For the reasons above, Applicants respectfully submit that neither a motivation to combine nor a reasonable expectation of successfully achieving the claimed invention exists with respect to New England Biolabs Products #1101-1108 and the Sumner, *et al.* reference. As a result, *prima facie* obviousness has not been established, and the instant 35 U.S.C. § 103 rejection should be withdrawn.

B. The Remaining Rejections and Objections.

Claims 94 and 95 stand rejected due to the phrase "consistently essentially of". While not agreeing with position stated in Paper 23, to advance prosecution Applicants above amended these claims by replacing the allegedly objectionable language with "comprising", thereby obviating this basis of rejection.

Regarding the rejection of and objection to claims 69-73, 76-80, 82, 83, 86-93, Applicants respectfully submit that the foregoing demonstration of non-obviousness of the claims from which these claims variously depend obviates these remaining issues.

### CONCLUSION

Herein, Applicants have amended certain of the pending claims and demonstrated the patentability of their claimed invention. Thus, a notice of allowance is earnestly solicited.

Should any matters remain outstanding, the Examiner is encouraged to telephone the undersigned so that the same can be resolved without the necessity for any additional formal action and response thereto.

Respectfully submitted,

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By:

A handwritten signature in black ink, appearing to read "Daniel M. Chambers", written over a horizontal line.

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